

SUPPLEMENTARY DATA

Supplementary Table S1. Demographic of participants at initial screening visit (N=48,026)

	Identical Twin N=288	Non-Identical Twin N=630	Full Sibling N=47,133	P value
Sex: Female	158 (55.1%)	296 (47.1%)	24,525 (52.4%)	0.019
Age at screening Median (IQR)	11.0 (7.0, 16.0)	10.0 (7.0, 14.0)	11.0 (7.0, 16.0)	0.002
Race/Ethnicity				0.043
White	231 (84.0)%	499 (81.0%)	35,880 (78.6%)	
Hispanic	20 (7.3%)	55 (8.9%)	5,614 (12.3%)	
Black	11 (4.0%)	31 (5.0%)	1,721 (3.8%)	
Asian	3 (1.1%)	10 (1.6%)	749 (1.6%)	
Other	10 (3.6%)	21 (3.4%)	1,715 (3.8%)	
HLA DQA1*05:01 (DR3) Present	23 (65.7%)	11(44.0%)	794(47.2%)	0.089
HLA DR4*0302Present	19 (54.3%)	19 (76%)	1,018 (60.5%)	0.215
HLA DQA1*05:01 (DR3)/4*0302 Present	12 (4.2%)	8 (1.3%)	414 (0.9%)	<0.001
HLA DR2*0602 Present	0 (0%)	2 (8%)	78 (4.6%)	0.308

Data shown as N (%) unless specified otherwise

Supplementary Table S2. Characteristics of subjects followed in the monitoring phase of TrialNet Pathway to Prevention study (N=17,226)

	ITN = 157	NTN = 283	FSN = 16,786	P value
Age at Screening Median years (IQR)	10 (6.0, 13.0)	10 (6.0, 12.0)	9(6.0, 12.0)	0.010
Single autoantibody positive subjects	28 (17.8%)	22 (7.8%)	1,480 (8.8%)	<0.001
Multiple autoantibody positive subjects	32 (20.4%)	18 (6.4%)	927 (5.5%)	<0.001
Follow up Time: Median years(IQR)	2.04(0.87, 3.72)	1.99(1.02, 3.28)	2.15 (1.09, 3.99)	0.001
Development of Type 1 Diabetes	31 (20%)	17 (6%)	594 (4%)	<0.001

Data shown as N (%) unless specified otherwise

IT: Identical twin

NT: Non-identical twin

FS: Full Sibling

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Supplementary Table S3. Development of autoantibodies by sibling status (N=17226).

Variable	Hazard Ratio (95% CI)	P value
GADA as Outcome		
Age in years at screening	1.06 (1.06, 1.07)	<0.0001
Identical Twins	3.11 (2.41, 4.03)	<0.0001
Non-Identical Twins	1.06 (0.75, 1.51)	0.729
IA-2A as Outcome		
Age in years at screening	1.03 (1.02, 1.04)	<0.0001
Identical Twins	2.91 (2.01, 4.20)	<0.0001
Non-Identical Twins	0.87 (0.56, 1.34)	0.523
IAA as Outcome		
Age in years at screening	0.99 (0.98, 1.00)	0.131
Identical Twins	3.07 (1.88, 4.31)	<0.0001
Non-Identical Twins	0.78 (0.53, 1.14)	0.195

Full siblings are the reference group

Supplementary Table S4. Development of type 1 diabetes by sibling status (N=17226).

Variable	Hazard Ratio (95% CI)	P value
Type 1 Diabetes in Identical Twins as Outcome		
Age in years at screening	0.90 (0.83, 0.98)	0.016
Autoantibody positive	76.92 (10.31, 500.00)	<0.0001
Type 1 Diabetes in Non-Identical Twins as Outcome		
Age in years at screening	0.97 (0.86, 1.09)	0.602
Autoantibody positive	58.82 (16.13, 200.00)	<0.0001
Type 1 Diabetes in Full Siblings as Outcome		
Age in years at screening	0.97 (0.95, 0.98)	<0.0001
Multiple Autoantibody positive	125.00 (90.91, 142.86)	<0.0001
Single Autoantibody positive	28.57 (21.74, 38.46)	<0.0001

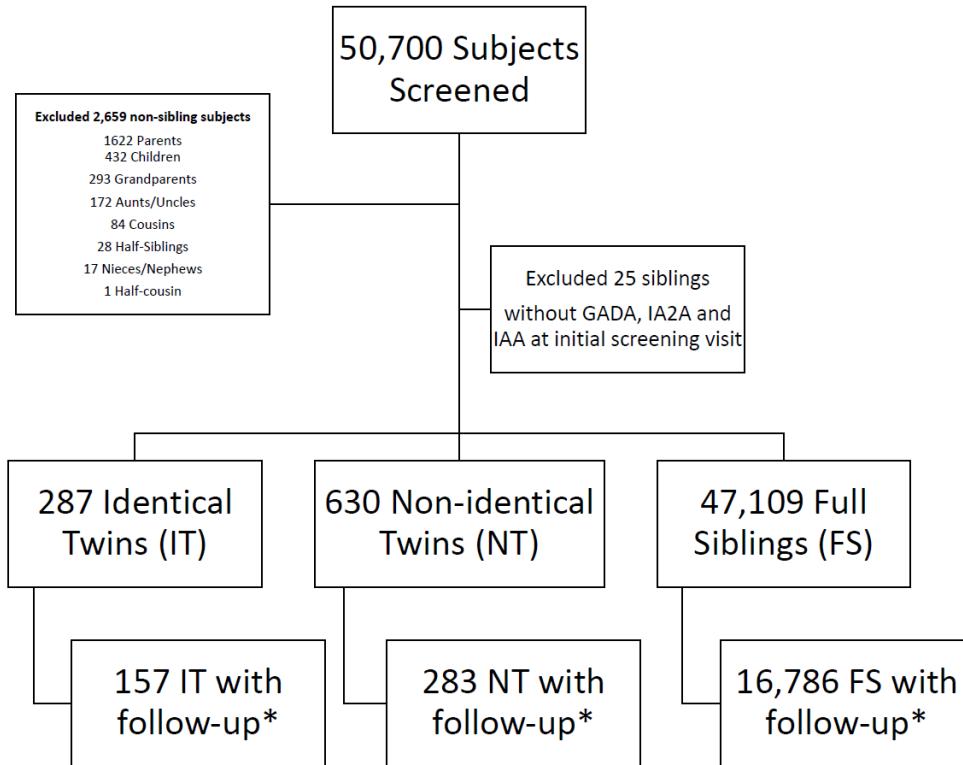
Effect of autoantibody positivity stratified by sibling status (N=17226).

Autoantibody negative siblings are the reference group

Cox Proportional Hazard Models Adjusted for Age

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Supplementary Figure S1. Flow chart of subject selection at screening and follow up



*Follow up: ≥ 12 months follow-up after initial screening visit

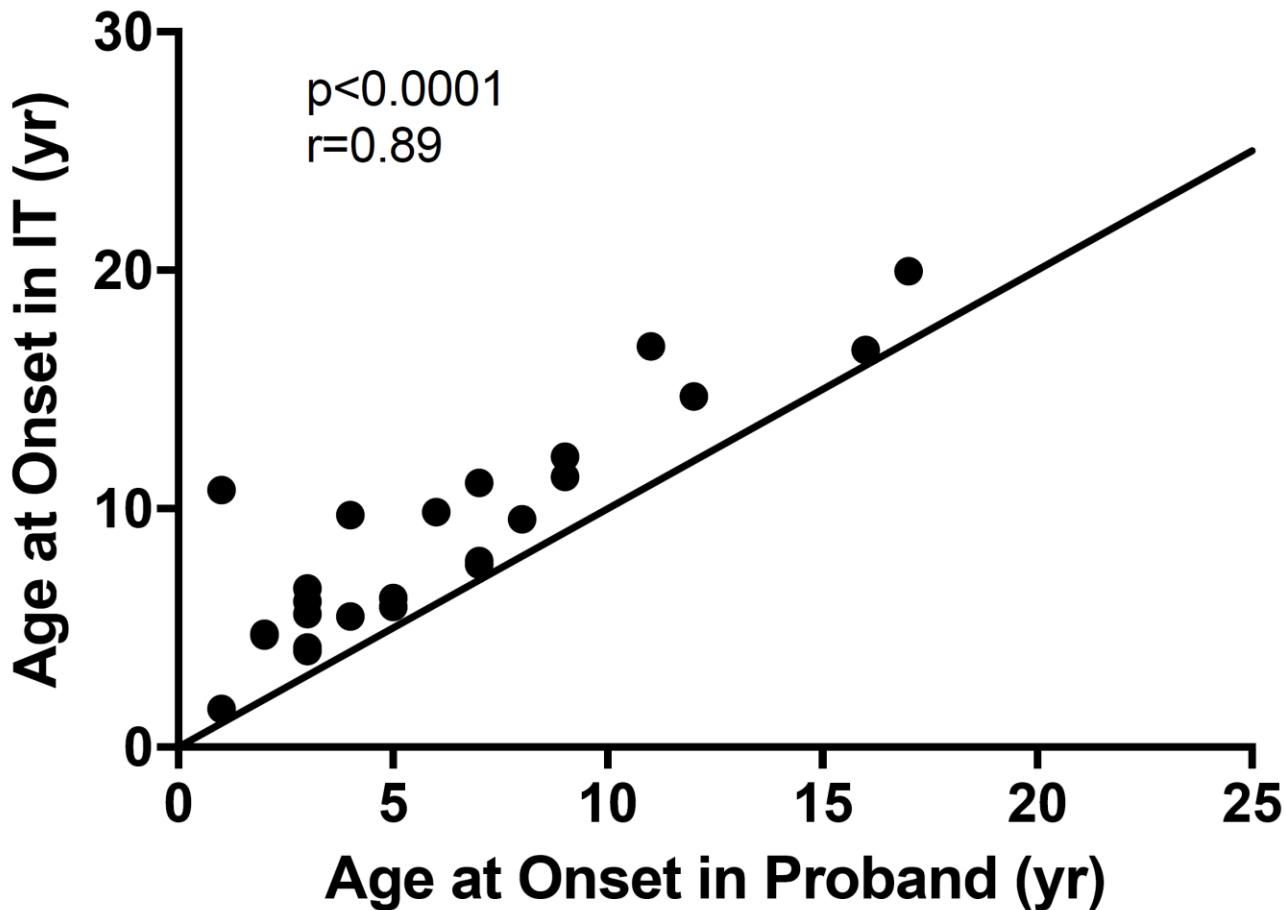
IT: identical twins

NT: non-identical twins

FS: full-siblings

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Supplementary Figure S2. Correlation of proband age of onset in years in identical twins (A) and non-identical twins (B)

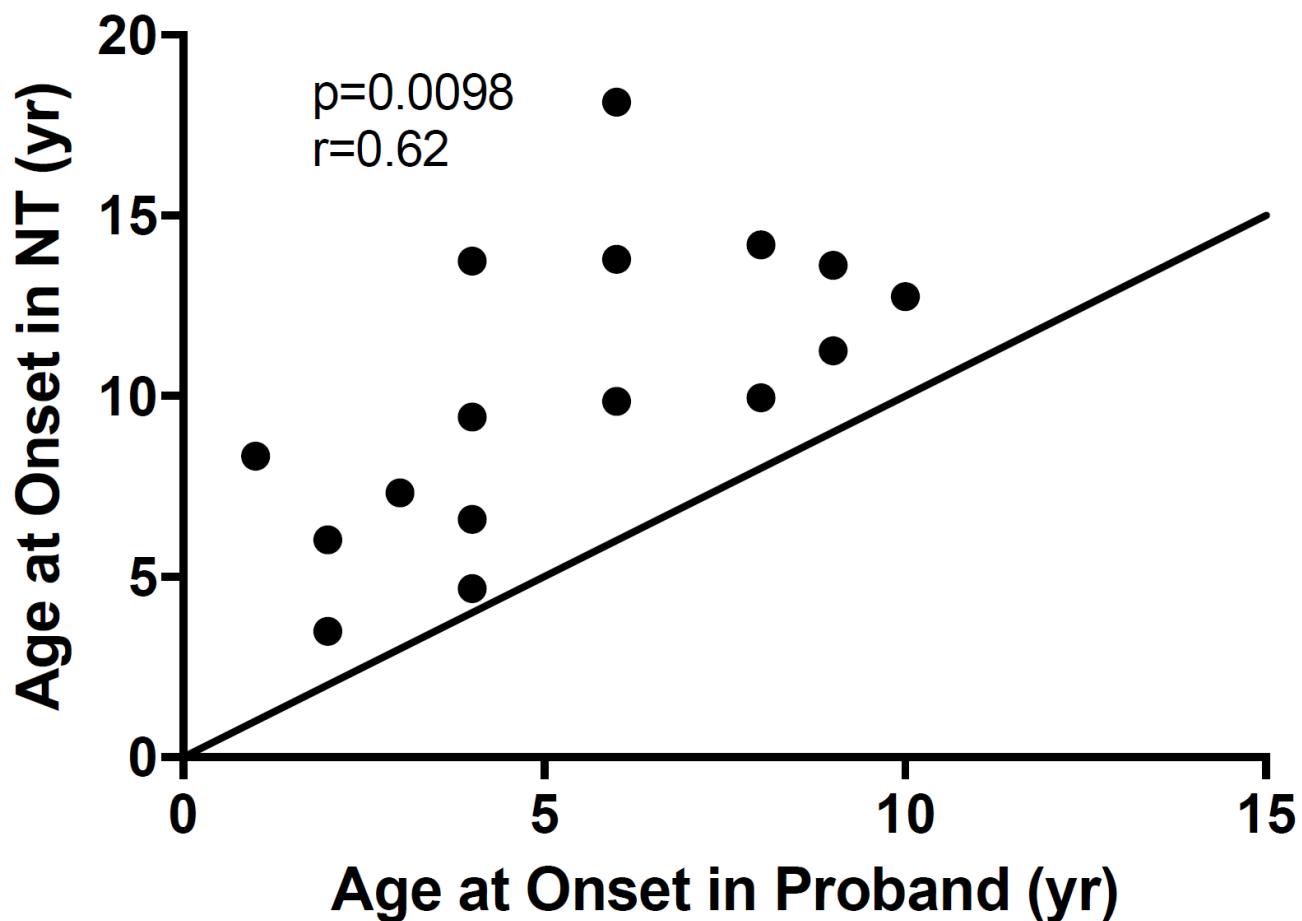


IT: identical twins

NT: non-identical twins

Yr: years

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IT: identical twins

NT: non-identical twins

Yr: years

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20160601 TrialNet On-line List of Affiliate Investigators.

TrialNet Affiliates: **Aberdeen, Scotland:** A. Mayo, J. Paxton, V. Thompson; Ajo, AZ- L. Volin; **Akron, OH-**C. Fenton, L. Carr, E. Lemon, M. Swank; **Albany, NY-**M.K. Luidens, M. Salgam, V. Sharma; **Albuquerque, NM-**D. Schade, C. King; Ames, IA-R. Carano, J. Heiden; **Anchorage, AK-**N.D. Means, L. Holman; **Ann Arbor, MI-**I. Thomas, D. Madrigal, T. Muth, C.L. Martin, C. Plunkett, C. Ramm, R.J. Auchus; **Asheville, NC-** W. Lane, E. Avots, M. Buford, C. Hale, J. Hoyle, B. Lane; **Atlanta, GA-**A. Muir, S. Shuler, N. Raviele, E. Ivie, M. Jenkins, K. Lindsley, I. Hansen, D.O. Fadoju, E.I. Felner, B. Bode, R. Hosey, J. Sax; **Auckland, NZ-**C. Jefferies, S. Mannerling, R. Prentis; Augusta, GA- J.X. She, M. Stachura, D. Hopkins, J. Williams, L. Steed, E. Asatapova; **Austin, TX-**S. Nunez, S. Knight, P. Dixon; Bakersfield, CA- J. Ching; **Baltimore, MD-**T. Donner, S. Longnecker, K. Abel, K. Arcara, S. Blackman, L. Clark, D. Cooke, L. Plotnick, P.A. Levin, L. Bromberger, K. Klein; **Bangor, ME-** K. Sadurska, C. Allen, D. Michaud, H. Snodgrass; **Bartlett, TN-**G. Burghen, S. Chatha, C. Clark; **Baton Rouge, LA-**J. Silverberg, C. Wittmer, J. Gardner, C. LeBoeuf; **Belfast, Ireland-**P. Bell, O. McGlore, H. Tennet, N. Alba; **Bend, OR-** M. Carroll, L. Baert, H. Beaton, E. Cordell, A. Haynes, C. Reed, K. Lichter, P. McCarthy, S. McCarthy, T. Monchamp, J. Roach, S. Manies; **Billings, MT-**F. Gunville, L. Marosok, T. Nelson, K. Ackerman, J. Rudolph, M. Stewart; **Birmingham, AL-**K. McCormick, S. May, T. Falls; **Birmingham, UK-**T. Barrett, K. Dale, L. Makusha, C. McTernana, K. Penny-Thomas, K. Sullivan, P. Narendran, J. Robbie, D. Smith; **Boise, ID-**R. Christensen, B. Koehler, C. Royal, T. Arthur, H. Houser, J. Renaldi, S. Watsen; **Bonita, CA-**P. Wu, L. Lyons, B. House, J. Yu; **Bournemouth, UK-**H. Holt, M. Nation, C. Vickers, R. Watling; Bronx, NY-R. Heptulla, J. Trast, C. Agarwal, D.J. Newell, R. Katikaneni; **Brunley, UK-**C. Gardner, A. Del Rio, A. Logan, H. Collier, C. Rishton, G. Whalley, A. Ali, S. Ramtoola; **Buffalo, NY-**T. Quattrin, L. Mastrandea, A.J. House, M. Ecker; Calgary, AB-C. Huang, C. Gougeon, J. Ho, D. Pacuad; **Cambridge, UK-**D. Dunger, J. May, C. O'Brien, C. Acerini, B. Salgin, A. Thankamony, R. Williams; Chapel Hill, NC- J. Buse, G. Fuller, M. Duclos, J. Tricome, H. Brown, D. Pittard; **Charleston, SC-**D. Bowlby, A. Blue, T. Headley; Charleston, WV-S. Bendre, K. Lewis, K. Sutphin; **Charlottesville, VA-**C. Soloranzo, J. Puskaric, H. Madison; **Chattanooga, TN-**M. Rincon, M. Carlucci, R. Shridharani, B. Rusk, E. Tessman, D.M. Huffman, H. Abrams, B. Biederman, M.D. Jones, V. Leathers; **Chicago, IL-**W. Brickman, P. Petrie, D. Zimmerman, J. Howard, L. Miller, R. Alemzadeh, D.V. Mihailescu, R. Melgozza-Walker, N. Abdulla, C. Boucher-Berry, D. Ize-Ludlow, R. Levy, C. Swenson Brousell; **Christchurch, NZ-**R. Scott, H. Heenan, H. Lunt, D. Kendall, J. Willis, B. Darlow; **Cincinnati, OH-**N. Crimmins, D. Edler, T. Weis, C. Schultz; **Cleveland, OH-**D. Rogers, D. Latham, C. Mawhorter, C. Switzer, W. Spencer, P. Konstantopoulos, S. Broder, J. Klein; **Colombia, MO-**B. Bachrach, M. Gardner, D. Eichelberger; **Columbia, SC-**L. Knight, L. Szadek, G. Welnick, B. Thompson; **Colombus, OH-**R. Hoffman, A. Revell, J. Cherko, K. Carter, E. Gilson, J. Haines, G. Arthur, B. Bowen, W.B. Zipf, P. Graves, R.A. Lozano, D. Seiple, K. Spicer; **Concord, CA-**A. Chang, J. Fregosi, J. Harbinson, C. Paulson, S. Stalters, P. Wright, D. Zlock; **Cooperstown, NY-**A.E. Freeth, J. Victory; **Crystal Lake, IL-** H. Maheshwari, A. Maheshwari, T. Holmstrom, J. Bueno; **Danbury, CT-**R. Arguello, J. Ahern, L. Noreika, V. Watson, S. Hourse; Dayton, OH-P. Breyer, C. Kissel, Y. Nicholson, M. Pfeifer, S. Almazan; **Denver, CO-**J. Bajaj, M. Quinn, K. Funk, J. McCance, E. Moreno, R. Veintimilla, A. Wells; **Des Moines, IA-**J. Cook, S. Trunnel; **Detroit, MI-**D. Transue, J. Surhigh, D. Bezzaire, K. Moltz, E. Zacharski; **Downers Grove, IL-** J. Henske, S. Desai, K. Frizelis, F. Khan; **Duluth, MN-**R. Sjoberg, K. Allen; **Dunedin, NZ-**P.P. Manning, G. Hendry, B. Taylor, S. Jones; **Edmonton, AB-**R. Couch, R. Danchak, D. Lieberman; **El Paso, TX-**W. Strader, M.E. Bencomo; **Escondido, CA-**T. Bailey, L. Bedolla, C. Roldan; **Exeter, UK-**C. Moudiotis, B. Vaidya, C. Anning, S. Bunce, S. Estcourt, E. Folland, E. Gordon, C. Harrill, J. Ireland, J. Piper, L. Scaife, K. Sutton, S. Wilkins, M. Costelloe, J. Palmer; **Fargo, ND-** L. Casas, C. Miller, M. Burgard, C. Erickson, J. Hallanger-Johnson; Florence, SC-P. Clark, W. Taylor; **Florissant, MO-** J. Galgani; Fresno, CA- S. Banerjee, C. Banda, D. McEowen, R. Kinman; **Garran, Australia-**A. Lafferty, S. Gillett, C. Nolan, M. Pathak; **Grand Folks, ND-**L. Sondrol, T. Hjelle, S. Hafner, J. Kotrba, R. Hendrickson; **Grand Rapids, MI-**A.P. Cemeroglu, T. Symington, M. Daniel, Y. Appiagyei-Dankah, D.C. Postellon, M.S. Racine, L. Kleis; **Greenville, NC-**K. Barnes, S.E. Godwin, H. McCullough, K. Shaheen, G. Buck, L. Noel, M.L. Warren; **Greenville, SC-**S. Weber, S.M. Parker, I. Gillespie, B.A. Nelson, C. Frost, J. Amrhein, E.C. Moreland, A. Hayes, J. Peggram; **Hackensack, NJ-** J. Aisenberg, M.E. Riordan, J. Zasa; **Halifax, NS-** E. Cummings, K. Scott, T. Pinto, A. Mokashi; **Hamilton, ON-** K. McAssey, E. Helden; **Harrogate, UK-**P. Hammond, L. Dinning, S. Rahman, S. Ray; **Hartford CT-** C. Dimicri, S. Guppy, H. Nielsen; Henderson, NV- C.K. Vogel, C. Ariza, L. Morales; **Hershey, PA-**Y.T. Chang, R.A. Gabbay, L. Ambrocio, L. Manley; **Hollywood, FL-** R. Nemery, W. Charlton, P. Smith, L. Kerr, B. Steindel-Kopp, M. Alamaguier; **Honolulu, HI-** E. Tabisola-Nuesca, A. Pendersen, N. Larson, H. Cooper-Olivier, D. Chan, D. Fitz-Patrick, T. Carreira, Y. Park, R. Ruhaak; **Idaho Falls, ID-** D. Liljenquist, G. Browning, T. Coughenour, M.B. Sulk; **Iowa City, IA-** E. Tsalikan, M. Tansey, J. Cabbage; **Jackson, MS-** N. Dixit, S. Pasha, M. King, K. Adcock, H. Atterberry; **Jacksonville, FL-** L. Fox, K. Englert, N. Mauras, J. Permuy, K. Sikes; **Joliet, IL-** T.

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Berhe, B. Guendling, L. McLennan, L. Paganessi, C. Murphy;Kalamazoo, MI- M.B. Draznin, M. Kamboj, S. Sheppard;**Kalispell, MT-** V. Lewis, L. Coates;**Kansas City, MO-** W. Moore, G. Babar, J. Bedard, D. Brenson-Hughes, J. Cernich, M. Clements, R. Duprau, S. Goodman, L. Hester, L. Huerta-Saenz, A. Karmazin, T. Letjen, S. Raman; **Kingsport, TN-** D. Morin, W. Bestermann, E.J. Morawski, J.L. White, A. Brockmyer, R. Bays, S. Campbell, A. Stapleton, N. Stone, A. Donoho, H. Everett, H. Hensley, M. Johnson, C. Marshall, N. Skirvin, P. Taylor, R. Williams, L. Ray, C. Wolverton;**Knoxville, TN-** D.A. Nickels, C. Dothard;**Lake Success, NY-** P.W. Speiser, M. Pellizzari, L. Bokor; **Las Vegas, NV-** K. Izuora, S. Abdelnour, P. Cummings, S. Paynor, M. Leahy, M. Riedl, S. Shockley, R. Saad, T. Briones;**Lebanon, NH-** S. Casella, C. Herz, K. Walsh;**Leicester, UK-** J. Greening, F. Hay, S. Hunt, N. Sikotra, L. Simons;**Lexington, KY-** D.G. Karounos, R. Oremus, L. Dye, L. Myers, D. Ballard, W. Miers, R. Sparks;**Little Rock, AR-** K.M. Thraikill, K. Edwards, J. Fowlkes, S. Kemp, A. Morales, L. Holland, L. Johnson;**Liverpool, UK-** P. Paul, A. Ghatak, K. Phelen, H. Leyland, T. Henderson;**Livingston, NJ-** D. Brenner, E. Oppenheimer, I. Mamkin, C. Moniz;**London, ON-** C. Clarson, M. Lovell;Los Angeles, CA- A. Peters, V. Ruelas, D. Borut, D. Burt, M. Jordan, S. Castilla, P. Flores, M. Ruiz, L. Hanson, J. Green-Blair, R.J. Sheridan;**Louisville, KY-** K.A. Wintergerst, G. Pierce, A. Omoruyi, M. Foster, S. Kingery;**Lubbock, TX-** A. Lunsford, I. Cervantes, T. Parker, P. Price, J. Urben;**Manchester, UK-** I. Doughty, H. Haydock, V. Parker;**Melbourne, Australia-** P. Bergman, S. Duncum, C. Rodda;**Memphis, TN-** A.D. Thomas, R. Ferry, D. McCommon, J. Cockroft; **Mesa, AZ-** A. Perelman, R. Calendo; **Miami, FL-** C. Barrera, E. Arce-Nunez, Y. Martinez, M. De la Portilla, I. Cardenas, L. Garrido, M. Villar;**Milan, Italy-** R. Lorini, E. Calandra, G. D'Annuzio, K. Perri, N. Minuto, C. Rebora, R. Callegari;**Milwaukee, WI-** O. Ali, J. Kramer, B. Auble, S. Cabrera, P. Donohoue, R. Fiallo-Scharer, M. Hessner, P. Wolfgram, A. Kansra, N. Bettin, R. McCuller, A. Miller;**Mineola, NY-** S. Accacha, J. Corrigan, E. Fiore, R.L. Levine, T.A. Mahoney;**Montreal, QC-** C. Polychronakos, V. Gagne;**Morristown, NJ-** H. Starkman, M. Fox, D. Chin, F. Melchionne, L.A. Silverman;**New Brunswick, NJ-** I. Marshall, L. Cerracchio, J. Cruz, A. Viswanathan, J. Wilson;**New Orleans, LA-** S. Chalew, S. Valley, S. Layburn, A. Lala, P. Clesi, M. Genet, G. Uwaifo, A. Charron, T. Allerton, W. Cefalu, L. Melendez-Ramirez, R. Richards, C. Alleyn, E. Gustafson, M. Lizanna; **New Port Richey, FL-** J. Wahlen, S. Aleiwe, M. Hansen, H. Wahlen;**New York, NY-** C.J. Levy, A. Bonaccorso, R. Rapaport, Y. Tomer, D. Chia, M. Goldis, L. Iazzetti, M. Klein, C. Levister, L. Waldman, E. Wallach, M.O. Regelmann, Z. Antal, M. Aranda, C. Reynolds;**Newcastle Upon Tyne, UK-** N. Leech, D. Wake, C. Owens, M. Burns, J. Wotherspoon, A. Murray, K. Short, G. Curry, S. Kelsey, J. Lawson, J. Porter, S. Stevens, E. Thomson, S. Winship, L. Wynn;Newton, NZ- E. Wiltshire, J. Krebs, P. Cresswell, H. Faherty, C. Ross;**Norfolk, VA-** A. Vinik, P. Barlow, M. Bourcier, M.L. Nevoret;**North Adelaide, Australia-** J. Couper, S. Beresford;**Norwich, UK-** N. Thalagne, H. Roper, J. Gibbons, J. Hill, S. Balleaut, C. Brennan, J. Ellis-Gage, L. Fear, T. Gray, L. Jones, C. McNerney, L. Pointer, N. Price, K. Few, D. Tomlinson;**Nottingham, UK-** L. Denvir, J. Drew, T. Randell, P. Mansell, S.A Bell, S. Butler, Y. Hooton, H. Navarra, A. Roper, G. Babington, L. Crate, H. Cripps, A. Ledlie, C. Moulds, R. Norton, B. Petrova, O. Silkstone, C. Smith; **Oak Lawn, IL-** K. Ghai, M. Murray, V. Viswanathan, M. Henegan, O. Kawadry;**Oakland, CA-** J.A. Olson, L. Patterson, T. Ahmad, B. Flores;**Oklahoma City, OK-** D. Domek, S. Domek, K. Copeland, M. George, J. Less, T. Davis, M. Short;**Olympia Fields, IL-** A. Dwarakanathan, P. O'Donnell;Omaha, NE- B. Boerner, L. Larson, M. Phillips, M. Rendell, K. Larson, C. Smith, K. Zebrowski, L. Kuechenmeister, M. Thevarayapillai;Orange, CA-M. Daniels, H. Speer, N. Forghani, R. Quintana, C. Reh, A. Bhangoo;**Orlando, FL-** P. Desrosiers, L. Ireland, T. Misla, C. Torres, S. Wells, J. Villar, M. Yu, D. Berry, D. Cook, J. Soder, A. Powell;**Ormskirk, UK-** M. Ng, M. Morrison, Z. Haslam;**Ottawa, ON-** M. Lawson, B. Bradley, J. Courtney, C. Richardson, C. Watson, E. Keely, D. DeCurtis; **Palm Beach Gardens, FL-** M. Vaccarello-Cruz, Z. Torres, K. Sandberg;**Pensacola, FL-** H. Hsiang, B. Joy, D. McCormick, A. Powell, H. Jones, J. Bell, S. Hargadon, S. Hudson, M. Kummer;**Peoria, IL-** S. Sauder, E. Sutton, K. Gensel, R. Aguirre-Castaneda, V. Benavides Lopez, D. Hemp, S. Allen, J. Stear;Perth, Australia- E. Davis, T. Jones, A. Roberts, J.A Dart, N. Paramalingam;**Philadelphia, PA-** L.E. Levitt Katz, N. Chaudhary; K.M. Murphy, S.M. Willi, B. Schwartzman;**Phoenix, AZ-** C. Kapadia, D. Larson, D. McClellan, G. Shaibai, L.A. Kelley, G. Villa, C. Kelley, R. Diamond, M. Kabbani, T. Dajani, F. Hoekstra, M. Magorno;**Pittsburgh, PA-** J. Holst, V. Chauhan, N. Wilson, P. Bononi, M. Sperl;**Plymouth, UK-** A. Millward, M. Eaton, L. Dean;**Portland, ME-** J. Olshan, H. Renna, C. Milliard;**Portland, OR-** D. Snyder, S. Beaman, K. Burch, J. Chester, A. Ahmann, B. Wollam, D. DeFrang, R. Fitch, K. Jahnke, K. Hanavan, B. Klopfenstein, L. Nicol, R.W. Bergstrom, T. Noland;**Poughkeepsie, NY-** J. Brodksy, L. Bacon;**Providence, RI-** J.B. Quintos, L.S. Topor, S. Bialo, B. Bancroft, A.G. Soto;**Raleigh, NC-** W. Lagarde, H. Lockemer, T. Vanderploeg; **Rancho Cucamonga, CA-** M.A Ibrahim, M. Huie, V. Sanchez; **Rapid City, SD-** R. Edelen, R. Marchiando, J. Palmer, T. Repas, M. Wasson, P. Auker, J. Culbertson, T. Kieffer, D. Voorhees, T. Borgwardt, L. DeRaad;**Reno, NV-** K. Eckert; **Richland, WA-** E. Isaacson, H. Kuhn, A. Carroll, M. Schubert;**Richmond, VA-** G. Francis, S. Hagan, T. Le, M. Penn, E. Wickham; **Rio Piedras, PR-** C. Leyva, K. Rivera, J. Padilla, I. Rodriguez;**Rochester, NY-** N. Jospe, J. Czyzyk, B. Johnson;**Sacramento, CA-** U. Nadgir, N. Marlen, G. Prakasam, C. Rieger, N. Glaser, E.C. Heiser, B. Harris;**Salt Lake City, UT** C. Foster, H. Slater, K. Wheeler, D.L Donaldson, M. Murray;**San Antonio, TX-** D.E. Hale, R. Tragus, D.R. Word, J. Lynch, L. Pankratz,

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W. Rogers; **San Diego, CA**- R. Newfield, S. Holland, M. Hashiguchi, M. Gottschalk, A. Philis-Tsimikas, R. Rosal, S. Franklin, S.M. Guardado; **San Francisco, CA**- N. Bohannon, M. Garcia; **San Jose, CA**- T. Aguinaldo, J. Phan, V. Barraza, D. Cohen; **Santa Barbara, CA**- J. Pinsker, U. Khan, J. Wiley, L. Jovanovic; **Santa Clara, CA**- P. Misra, M. Wright, D. Cohen, K. Huang; **Scottsbluff, NE**- M. Skiles, S. Maxcy; **Seattle, WA**- C. Pihoker, K. Cochrane, J. Fosse, S. Kearns, M. Klingsheim; **Sheffield, UK**- N. Wright, L. Viles, H. Smith, S. Heller, M. Cunningham, A. Daniels, L. Zeiden, J. Field, R. Walker; **Sioux Falls, SD**- K.J. Griffin, L. Bartholow, C. Erickson, J. Howard, B. Krabbenhoft, C. Sandman, A. Vanveldhuizen, J. Wurlger, A. Zimmerman, K. Hanisch, L. Davis-Keppen; **South Brisbane, Australia**- A. Cotterill, J. Kirby, M. Harris, A. Schmidt; **Spokane, WA**- C. Kishiyama, C. Flores, J. Milton, W. Martin, C. Whysham, A. Yerka, T. Freels, J.M. Hassing, J. Webster; **Springfield, IL**- R. Green, P. Carter, J. Galloway, D. Hoelzer, S. Roberts, S. Said, P. Sullivan; **Springfield, MA**- H.F. Allen, E. Reiter, E. Feinberg, C. Johnson; **St. John's, NL**- L.A. Newhook, D. Hagerty; **St. Louis, MO**- N.H. White, L. Levandoski; **St. Paul, MN**- J. Kylo, M. Johnson, C. Benoit; **St. Petersburg, FL**- P. Iyer, F. Diamond, H. Hosono, S. Jackman, L. Barette, P. Jones; **Syracuse, NY**- I. Sills, S. Bzdick, J. Bulger, R. Weinstock; **Taunton, UK**- I. Douek, R. Andrews, G. Modgill, G. Gyorffy, L. Robin, N. Vaidya, S. Crouch, K. O'Brien, C. Thompson, N. Thorne; **Toledo, OH**- J. Blumer, J. Kalic, L. Klepek, J. Paulett, B. Rosolowski, J. Horner, M. Watkins; **Topeka, KS**- J.L. Casey, K. Carpenter, C. Burns, J. Horton, C. Pritchard, D. Soetaert, A.G. Wynne; **Torrance, CA**- K. Kaiserman, M. Halvorson; **Tucson, AZ**- C. Chin, O.Y. Molina, C. Patel, R. Senguttuvan, M. Wheeler, O. Furet, C. Steuhm; **Tulsa, OK**- D.H. Jolley, S. Goudeau, L. Chalmers, D. Greer; **Vancouver, BC**- C. Panagiotopoulos, D.L. Metzger, D. Nguyen, M. Horowitz; **Walnut Creek, CA**- M.P. Christiansen, E. Glades, C. Morimoto, M. Macarewich, R. Norman, K. Patin, C. Vargas, A. Barbanica, A. Yu; **Washington D.C.**- P. Vaidyanathan, W. Osborne, R. Mehra; **Wenatchee, WA**- S. Kaster, S. Neace, J. Horner; **Wilmington, DE**- G. Reeves, C. Cordrey, L. Marrs, T. Miller, S. Dowshen, D. Doyle; **Winnipeg, Manitoba**- S. Walker, D. Catte, H. Dean; **Winston-Salem, NC**- M. Drury-Brown, B. Hackman; **Worcester, MA**- M.M.C Lee, S. Malkani, K. Cullen, K. Johnson; **Yuma, AZ**- P. Hampton, M. McCarrell, C. Curtis, E. Paul, Y. Zambrano.

Type 1 Diabetes TrialNet Study Group

Steering Committee: C. J. Greenbaum, Chair (Benaroya Research Institute), M. Atkinson (University of Florida), D. Baidal (University of Miami), M. Battaglia (San Raffaele Diabetes Research Institute), D. Becker (University of Pittsburgh), P. Bingley (University of Bristol), E. Bosi (San Raffaele University), J. Buckner (Benaroya Research Institute), M. Clements (Children's Mercy Hospital), P. Colman (Walter & Eliza Hall Institute of Medical Research), L. DiMeglio (Indiana University), S. Gitelman, (University of California, San Francisco), R. Goland (Columbia University), P. Gottlieb (University of ColoradoBarbara Davis Center for Childhood Diabetes), K. Herold (Yale University), M. Knip (University of Helsinki), J. Krischer (University of South Florida), A. Lernmark (Skane University), W. Moore (Children's Mercy Hospital), A. Moran (University of Minnesota), A. Muir (Emory University), J. Palmer (University of Washington), M. Peakman (King's College), L. Philipson (University of Chicago), P. Raskin (University of Texas Southwestern), M. Redondo (Baylor University), H. Rodriguez (University of South Florida), W. Russell (Vanderbilt University), L. Spain (National Institute of Diabetes and Digestive and Kidney Diseases [NIDDK]), D.A. Schatz (University of Florida), J. Sosenko (University of Miami), J. Wentworth (Walter & Eliza Hall Institute of Medical Research), D. Wherrett (University of Toronto), D. Wilson (Stanford University), W. Winter (University of Florida), A. Ziegler (Technical University Munich). Previous Members: M. Anderson (University of California, San Francisco), P. Antinozzi (Wake Forest University), C. Benoist (Joslin Diabetes Center), J. Blum (Indiana University), K. Bourcier, P. Chase (University of ColoradoBarbara Davis Center for Childhood Diabetes), M. Clare-Salzler (University of Florida), R. Clynes (Columbia University), G. Eisenbarth (University of ColoradoBarbara Davis Center for Childhood Diabetes), C. G. Fathman (Stanford University), G. Grave (National Institute of Child Health and Human Development), B. Hering (University of Minnesota), R. Insel (Juvenile Diabetes Research Foundation), F. Kaufman (Children's Hospital Los Angeles), T. Kay (St Vincent's Institute of Medical Research), E. Leschek (NIDDK), J. Mahon (University of Western Ontario), J.B. Marks (University of Miami), K. Nanto-Salonen (University of Turku), G. Nepom (Benaroya Research Institute), T. Orban (Joslin Diabetes Center), R. Parkman (Children's Hospital Los Angeles), M. Pescovitz (Indiana University), J. Peyman (National Institute of Allergy and Infectious Disease), A. Pugliese (University of Miami), B. Roep (Leiden University Medical Center), M. Roncarolo (San Raffaele University), P. Savage (NIDDK), O. Simell (University of Turku), R. Sherwin (Yale University), M. Siegelman (University of Texas Southwestern), J.S. Skyler (University of Miami), A. Steck (University of ColoradoBarbara Davis Center for Childhood Diabetes), J. Thomas (Vanderbilt University), M. Trucco (University of Pittsburgh), J. Wagner (University of Minnesota).

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Executive Committee: Carla J. Greenbaum, Jeffrey P. Krischer, Ellen Leschek, Lisa Rafkin, Lisa Spain.Past Members: Katarzyna Bourcier, Catherine Cowie, Mary Foulkes, Richard Insel, Heidi Krause- Steinrauf, John M. Lachin, Saul Malozowski, John Peyman, John Ridge, Peter Savage, Jay S. Skyler, Stephanie J. Zafonte.

Chairman's Office: Carla J. Greenbaum, Lisa Rafkin, Jay M. Sosenko.Past Member: Jay S. Skyler, Norma S. Kenyon, Irene Santiago.

TrialNet Coordinating Center (University of South Florida): Jeffrey P. Krischer, Brian Bundy, Michael Abbondondolo, Timothy Adams, Ilma Asif, Matthew Boonstra, Brian Bundy, David Cuthbertson, Christopher Eberhard, Steve Fiske, Julie Ford, Jennifer Garmeson, Heather Guillette, Susan Geyer, Brian Hays, Courtney Henderson, Martha Henry, Kathleen Heyman, Belinda Hsiao, Kaleena Dezzi, Christina Karges, Amanda Kinderman, Ashley Leinbach, Lindsay Lane, Shu Liu, Jennifer Lloyd, Jamie Malloy, Kristin Maddox, Julie Martin, Jessica Miller, Eric Milliot, Margaret Moore, Sarah Muller, Thuy Nguyen, Jodie Nunez, Ryan O'Donnell, Melissa Parker, MJ Pereyra, Nichole Reed, Tina Stavros, Roy Tamura, Keith Wood, Rebessa Wood, Ping Xu, Kenneth Young.Past Staff Members: Persida Alies, Darlene Amado, Franz Badias, Aaron Baker, Monica Bassi, Craig Beam, David Boulware, London Bounmananh, Susan Bream, Cristina Burroughs, Mary Deemer, Doug Freeman, Jessica Gough, Jinin Ginem, Moriah Granger, Mary Holloway, Michelle Kieffer, Page Lane, Pat Law, Cristin Linton, Lavanya Nallamshetty, Vanessa Oduah, Yazandra Parrimon, Kate Paulus, Jennifer Pilger, Joy Ramiro, AQesha Luvon Ritzie, Amy Roberts, Kelly Sadler, Archana Sharma, Audrey Shor, Xiaohong Song, Amanda Terry, Jeanne Weinberger, Margaret Wootten.

Previous Coordinating Center (George Washington University): John M. Lachin, Mary Foulkes, Pamela Harding, Heidi Krause-Steinrauf, Susan McDonough, Paula F. McGee, Kimberly Owens Hess, Donna Phoebus, Scott Quinlan, Erica Raiden.

TrialNet Clinical Network HUB (Benaroya Research Institute): Carla J. Greenbaum, Emily Batts, Chris Buddy, Julie Hunt, Kristin Kirpatrick, Mary Ramey, Ann Shultz, Chris Webb, Past Member: Melita Romesco.

NIDDK Staff: Judith Fradkin, Ellen Leschek, Lisa Spain. Past Member: Peter Savage.

Data Safety and Monitoring Board: Sean Aas (Georgetown University), Emily Blumberg (University of Pennsylvania), Chair, Gerald Beck (Cleveland Clinic), Rose Gubitosi-Klug (Case Western Reserve), Lori Laffel (Joslin Diabetes Center), Sean Aas (Georgetown University), Robert Vigersky (Medtronic), Dennis Wallace (Research Triangle Institute).Past Members: Jonathan Braun (University of California Los Angeles), David Brillon (Cornell University), Ake Lernmark (Lund University), Bernard Lo (University of California San Francisco), Herman Mitchell (Rho Inc.), Ali Naji (University of Pennsylvania), Jorn Nerup (University of Copenhagen), Trevor Orchard (University of Pittsburgh), Michael Steffes (University of Minnesota), Anastasios Tsiatis (North Carolina State University), Robert Veatch (Georgetown University), Bernard Zinman (University of Toronto).

Infectious Disease Safety Committee: Brett Loeffelt (Children's National Medical Center) (Medical Monitor), Lindsey Baden (Harvard University), Michael Green (University of Pittsburgh), Adriana Weinberg (University of Colorado).

Laboratory Directors: Santica Marcovina (University of Washington), Jerry P. Palmer, Adriana Weinberg, Liping Yu (University of Colorado Barbara Davis Center for Childhood Diabetes), Sunanda Babu (University of Colorado Barbara Davis Center for Childhood Diabetes) William Winter (University of Florida). Past Member: George S. Eisenbarth (late).

Protocol Chair Committee: Diane Wherrett, Polly Bingley, Linda DiMeglio, George Eisenbarth, Carla Greenbaum, Brian Hays, Jeffrey Krischer, Ellen Leschek, Della Matheson, Lisa Rafkin, Henry Rodriguez, Jay Sosenko, Lisa Spain, Darrell Wilson. Past Members: Raphael Clynes, Jennifer Marks, Jay Skyler.

Clinical Center Staff Involved in this Protocol:

Baylor College of Medicine: Maria Redondo, David Gomez, Andrene McDonald, Sandra Pena, Massimo Pietropaolo, Kathy Shippy.

SUPPLEMENTARY DATA

Benaroya Research Institute, Seattle: Carla Greenbaum, Emily Batts, Jane Buckner, Marissa Hammond, Wei Hao, Deborah Hefty, Sandra Lord, Marli McCulloch-Olson, Gerald Nepom, Mary Ramey, Jenna Snavely, Kimberly Stickney, Meghan Tobin, Corinna Tordillos, Dana VanBuecken, Nancy Wickstrom. Past Members: Laurie Allen, Jenna Bollyk, Tyler Brown, Angela Dove, Nicole Hilderman, Hebatullah Ismail, Jani Klein, Kristen Kuhns, Steve Lamola, McKenzie Letlau, Lisa Miller, Jared Odegard, Elaine Sachter, Srinath Sanda, Marissa St. Marie, David Tridgell, Heather Vendettuoli, Ben Vellek, Christine Webber.

Children's Hospital Los Angeles: Roshanak Monzavi, Daniel Bisno, Lynda Fisher, Brian Ichihara, Kevin Kwan, Jennifer Raymond,.Past Members:Meredith Bock, Mitchell Geffner, Mary Halvorson, Debra Jeandron, Francine Kaufman, Mimi Kim, Robertson Parkman,Christine Salazar,Jamie Wood, Alison Woods.

Columbia University, New York: Robin Goland, Magdalena Bogun, Rachelle Gandica, Sarah Pollak, Kristen Williams, Past Members:Thomas Brazda, Mary Chan, Raphael Clynes, Steve Cook, Matthew Freeby, Mary Pat Gallagher, Ellen Greenberg, Linda Koplimae, Amy Kurland, Elizabeth Levine, Zuleika Parra, Kim Pope, Kelly Smith, Jeniece Trast, Amy Wolk.

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Joslin Diabetes Center, Boston:Jason Gaglia, Christina Astley, Nora Bryant, Katharine Garvey, Suzanne Krischfield, Sarah Szubowicz, Jean Turley, Gordon Weir.Past Members:Cielo Alleyn, David Baidal, Steve Fay, Ronald Benjamin, Debbie Conboy, Andrea deManbey, Richard Jackson, Heyam Jalahej, Mary Ellen Migre, Tihmar Orban, Brittany Resnick, Alyne Ricker, Joseph Wolfsdorf, Hui H. Zhang.

Stanford University: Darrell Wilson, Nora Arrizon-Ruiz, Tandy Aye, Laura Bachrach, Bonita Baker, Karen Barahona, Trudy Esrey, Laura Nally, Parul Patel..Past Members: Beenu Aneja, Bruce Buckingham, Julia Buckingham, Kim Caswell, Christina Chau, Maya Chatav, Daniela DeSalvo, Oralia Espinoza, Garry Fathman, Eliana Frank, Rajiv Kumar, Claire Lande, Jenny Liu, Jennifer Perry, Rebecca Pyle, Alison Rigby, Kristin Riley, Avni Shah, Sejal Shah, Adriana Soto, Matthew Stenerson, .

University of CaliforniaSan Francisco: Stephen Gitelman, Mark Anderson, Glenna Auerback, Eric Bomberg, Jeanne Buchanan, Ayka Erkin-Cakmak, Christine Ferrara, Karen Ko, Janet Lee, Robert Long, Marcela Rodriguez, Srinath Sanda, Carolyn Spann, Christine Torok, Rebecca Wesch.Past Members:Saleh Adi, Ivy Aslan, Ashley Berhel, Kathy Breen, Jeanne Buchanan, Jennifer Cordier,Kathleen Fraser, Sheila Ghods, Andrea Gerard-Gonzalez, Lubna Hamid, Celia Hamilton, Louise Hawkins, Thu Ho, Alyssa Huang, Anjali Jain, Paula Jossan, Theresa Lee, Robert Lustig, Sara Moassesfar, Amy Mugg, David Ng, Colette O'Brian, Shelly Phelps, Priya Prahalod, Martha Rangel-Lugo, Tracy Rodriguez, Stephen Rosenthal,Bahar Sadjadi, Taninee Sahakitrungruang, Lorraine Stehl, Joshua Tarkoff, Lisa Taylor, Marcia Wertz, Jenise Wong.

University of Chicago: Louis Philipson, Diane Deplewski, Gail Gannon, Siri Greenley, Leeon Jones, Harini Kolluri, Michelle Lemelman, Kathy Mansell, Mary Miller, Rochelle Naylor, Katie O'Sullivan, Treniece Pearson, Mariko Pusinelli, Susan Tucker, Cynthia Warnes, Christine Yu. Past Members: Nancy Devine, Tiffany Grant, Lisa Letourneau, Elizabeth Littlejohn.

University of Colorado Barbara Davis Center for Childhood Diabetes, Aurora: Andrea Steck,Aimon Alkanani, Mayalin Barr, Kimberly Bautista, Betsy Burke, Mary Drye,Alex Fouts, Patricia Gesauldo, Peter Gottlieb, Raymond Gutin, Michelle Hoffman,Aaron Michels,Flor Sepulveda, Kimber Simmons, Andrea Steck, Iman Taki,R. Paul Wadwa.Past Members:Jennifer Barker, Sandra Barry, Ruth Bedoy, Laurie Birks, Leah Bomsburger, Terra Bookert, Carrie Brill, Leah Briggs, Patricia Burdick, Rosio Cabrera, Peter Chase, Erin Cobry,Amy Conley, Gabrielle Cook, Laraine Cory, MyLinh Dang, Joseph Daniels, Dominic DiDomenico, Jennifer Eckert, Angelica Ehler, George Eisenbarth (late), Pamela Fain, Rosanna Fiallo-Scharer,Lisa

SUPPLEMENTARY DATA

Fitzgerald-Miller, Natalie Fouts, Nicole Frank, Vicky Gage, Satish Garg, Hannah Goettle, Michelle Haarhues, Sherrie Harris, Cory Hayes, Lauren Horton, John Hutton (late), Joy Jeffrrey, Rachael Jenison, Kelly Jones, Whitney Kastelic, Kaitlin Ketchum, Maria Amelia King, Georgeanna Klingensmith, Debbie Lehr, Nyla Logsden-Sackett, Jenna Lungaro, David Maahs, Kendra Mason, Heather Maurer, Laurel Messer, Lisa Meyers, Luy Nguyen, Allison Proto, Jaime Realsen, Marian Rewers, Allison Schauwecker, Kristina Schmitt, Mara Schwartz, San Skovgaard, Jennifer Smith, Brandon Vanderwel, Mary Voelmle, Rebecca Wagner, Amy Wallace, Philip Walravens, Laurie Weiner, Becky Westerhoff, Emily Westfall, Katina Widmer, Hali Wright.

University of Florida, Gainesville: Desmond Schatz, Annie Abraham, Anastasia Albanese-O'Neill, Mark Atkinson, Brittany Bruggeman, Todd Brusko, Michael Clare-Salzler, Kristin Dayton, Michael Haller, Paul Hiers, Jennifer Hosford, Laura Jacobsen, John Marks, Henry Rohrs, Janet Silverstein, Paula Towe, William Winter, Chelsea Zimmerman. Past Members: Gloria Cole, Roberta Cook, Ryan Coy, Jessica Ferguson, Elena Hicks, Monet Johnson, Nancy Lewis, Diane Mancini, Colette Meehan, Bimota Nambam, Glenna Paguio, Socorro Pata, Eleni Sheehan, Jamie Thomas.

University of Miami: David Baidal, Carlos Blaschke, Della Matheson, Alberto Pugliese, Natalia Sanders-Branca, Jay Skyler, Jay Sosenko. Past Members: Luz Arazo Ray Arce, Mario Cisneros, Jennifer Marks, Samir Sabbag.

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University of Pittsburgh: Dorothy Becker, Kelli DeLallo, Ana Diaz, David Groscost, Heba Ismail, Mary Beth Klein, Ingrid Libman, Karen Riley. Past Members: Brian Copemen, Barbara Elnyczky, Diane Gwynn, Natalie Hecht Baldauff, Beata Pasek, Frederico Toledo, Massimo Trucco.

University of South Florida: Henry Rodriguez, Ciara Alvarex, Sureka Bollepalli, Jerry Brown, Rachel Brownstein, Alison Castro, Linda Deterding, Emily Eyth, Max Feldman, Rachel Franks, Danielle Gomez, Lucy Guerra, Rachelle Idziak, Crystal Jacobino, Verena Jorgensen, Byron Moran, Hugo Navarte, Asa Oxner, Dorothy Shulman, Amanda Terry. Past Members: Craig Bobik, Frank Diamond, Danielle Henson, Pallavilyer, Michelle Laine, Anne Lenz, Jennifer Steinbreuck, Sheryl Tindell.

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University of Toronto: Diane Wherrett, Danyella Dias, Lesley Eisel, Roze Kovalakovska, Bianca Perro, Mary Jo Ricci. Past Members: Brenda Ahenkorah, Jose Cevallos, Samantha DeLima, Mala Mehan, Mark Parmert, Natasha Razack, Angela Roode, Mithula Srikantharajah, Farah Sultan, Rachel Steger.

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Yale University, New Haven: Kevan Herold, Laurie Feldman, Jennifer Sherr, Robert Sherwin, William Tamborlane, Stuart Weinzimer. Past Members: Kim Kunze, Frank Waldron-Lynch.

International Clinical Center Staff involved in this Protocol:

SUPPLEMENTARY DATA

Hospital District of Southwest (Finland): Jorma Toppari, Annika Adamsson, Sanna Jokipuu, Leena Karlsson, Jukka Kero, , Birgitta Nurmi, Petro Rajala, Eeva Ruohonen. Past Members: Kirsti Näntö- Salonen, Tiina Niininen Olli Simell, Satu Simell, Tuula Simell, Sointu Suomenrinne, Maija Torma, Johanna Walkback.

San Raffaele Hospital (Italy): Emanuele Bosi, Manuela Battaglia, Eleonora Bianconi, Andrea Bolla, Clara Bonura, Amelia Caretto, Giulio Frontino, Pauline Grogan, Andrea Laurenzi, Sabina Martinenghi, Chiara Molinari, Matteo Pastore, Alessandra Petrelli. Past Members: Riccardo Bonfanti, Franco Meschi, Maria Teresa Muscato, Matteo Viscardi.

Skane University Hospital (Sweden): Ake Lernmark, Markus Lundgren, Ulrika Ulvenhag. Past Members: Jessica Melin, Hindrik Mulder, Caroline Nilsson, Anders Rosengren, Birgitta Sjoberg, Hanna Skarstrand, Anne Wallin, Asa Wimar.

Technical University Munich (Germany): Anette-G. Ziegler, Peter Achenbach, Susanne Aydin, Melanie Bunk, Alevtina Durmashkina, Melanie Heinrich, Melanie Herbst, Susanne Hivner, Magdalena Kroetz, Claudia Ramminger, Katharina Warncke. Past Members: Ruth Chmiel, Florian Haupt, Anna Hofelich, Nadezha Lagoda, Nicole Maison, Ester Mau, Christian Sebelefsky, Marcus Walter.

University of Bristol (United Kingdom): Polly Bingley, Chloe Gillum, Tracey Hughes, Yuk-Fun Liu, Sam Loud, Beth Thorne. Past Members: Harriet Castleden, Rebecca Elliot-Jones, Nicola Farthing, Claire Matthews, Caroline Pope, Clemence Rouquette.

University of Helsinki (Finland): Mikael Knip, Minna Hirvasniemi, Susanne Johansson, Katrina Koski, Kristina Luopajarvi, Heli Siljander, Heli Suomalainen. Past members: Matti Hero, Eeva Jaon, Paivi Kalliola, Paivi Keskinen, Marja-Leena Koski, Marti Koski, Merja Koskinen, Tarja Laamanen, Suvia Laurinen, Taina Mustila, Miia Pekkola, Marja-Tertta Saha, Kirsi Salonen, Jenni Selvenius.

Walter and Eliza Hall Institute of Medical Research (Australia): Peter Colman, Candice Breen, Spiros Fourlanos, Leonard Harrison, Felicity Healy, Leanne Redl, John Wentworth, Jinny Willis. Past Members: Narika Bjarasen, Nicola Dalgleish, Maree Farley, Jane French, Felicity McManus, Shelley Mesfin, Christine Perry, Jennie Pfeiffer, Fiona Williams.